REMARKS

Review and reconsideration on the merits are requested.

Basis for Amendments

Claim 1 has been amended to include the subject matter of claims 5, 6, 7 and 10 in limited dosage form to a capsule. Support for partially pregelatinized starch occurs at page 13, line 8 and for sodium lauryl sulfate at page 19, lines 18 and 19. Support for the capsule concept occurs at page 19, lines 9-26. Examples of embodiments of the capsule of claim 1 are specifically disclosed in Examples 1 and 2 in the specification.

Formalities

Applicants appreciate the Examiner returning initialed PTO/SB/08 filed June 9, 2005.

Claim Rejections - 35 U.S.C. § 112

The formula in claim 1 is relocated so that now there is a formula after the colon on line 3 of claim 1.

Withdrawal is requested.

The Prior Art

U.S. 5,387,603 Kitazawa et al (Kitazawa); U.S. 2002/0177593 Ishihara et al (Ishihara);

The Rejections

Claims 1-4 and 16-18 under 35 U.S.C. § 102(b) as anticipated by Kitazawa.

Claims 1-12 and 14-26 under 35 U.S.C. § 103(a) as unpatentable over Kitazawa in view of Ishihara.

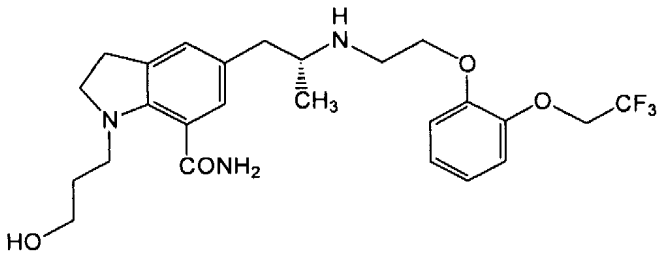
The Examiner's reading of the prior art and application to the claims as set forth in the Action and will not be repeated here except as necessary to an understanding of Applicants' traversal which is now presented.

Traversal

Claim 1 is now directed to:

A capsule, which comprises:

(1) a granular material containing a) as an active ingredient, an indoline compound represented by the formula:



b) D-mannitol and c) partially pregelatinized starch; and

(2) d) a lubricant selected from magnesium stearate, calcium stearate or talc, and e) sodium lauryl sulfate,

wherein 85% dissolution time is not more than 15 minutes in a dissolution test according to method 2 (paddle method) of Japanese pharmacopoeia in a condition using water as a test medium and a paddle speed of 50rpm.

The capsule of the present invention exhibits very quick dissolution in water in which the active ingredient of KMD-3213 is hardly soluble, and has excellent therapeutic activity for the treatment of dysuria. The capsule of the present invention also shows excellent storage stability and high filling precision where variation in the contained amount of the active ingredient is very little. The capsule of the present invention is suitable for industrial production.

Such advantageous effects of the present invention were firstly achieved by the above features of claim 1 where a capsule comprises 1) a granular material containing a) KMD-3213 as an active ingredient, b) D-mannitol and c) partially pregelatinized starch, and 2) d) a lubricant selected from magnesium stearate, calcium stearate or talc and e) sodium lauryl sulfate.

Kitazawa et al

Kitazawa discloses the compound KMD-3213 which is useful as a therapeutic agent for treating dysuria (cols. 49 to 50 as Compound 40). However, Kitazawa does not specifically disclose the capsule of the present invention. Kitazawa also fails to teach or suggest the capsule of the present invention or the advantageous effects of the capsule of the present invention.

Ishihara

Ishihara discloses several formulation examples on page 51, and pages 55 to 56 as Formulation examples 1 to 6 in the specification. The formulations are all tablets containing a) lactose, b) corn starch and c) magnesium stearate. The dosage forms and compositions of Formulation examples 1 to 6 are all quite different from those of the capsule of the present invention.

Ishihara also makes general mention regarding Formulations, Administration Routes and Dosages on pages 43 to 46 and teaches a variety of organic or inorganic carrier materials conventionally employed as pharmaceutical materials such as bulking agents, lubricants, binders and disintegrants for solid preparations. A number of ingredients for each of the bulking agents, lubricants, binders, and disintegrants are listed in Ishihara.

However, Ishihara does not specifically disclose the capsule of the present invention. Ishihara also fails to teach or suggest the capsule of the present invention or the advantageous effects of the capsule of the present invention.

Distinction over Kitazawa in view of Ishihara

The Examiner states that:

"[Ishihara et al] teach that these agents can be administered in capsule or tablet form further comprising a light-shielding coating agent like titanium oxide, D-mannitol, magnesium

stearate, and sodium lauryl sulfate (see paragraphs [0618], [0626], [0620], and [0596]) on page 5, lines 15-18 in the Action.

However, Ishihara merely teaches that a number of ingredients listed for bulking agents, lubricants, binders, disintegrants, and suspending agents may be used for preparing capsules according to a conventional formulation technology.

The Examiner also states:

"The conventional molding methods would inherently include the dissolution time according to Japanese pharmacopoeia", on page 3, lines 15-17 in the Action, citing Ishihara at paragraph [0619]. Ishihara does state that "the pharmaceutical compositions can be produced according to a conventional method in the field of formulation technology, for example, a method described in the Japanese Pharmacopoeia or the like" at paragraph [06191 on page 45. However, this merely teaches that those skilled in the art could prepare formulations in accordance with conventional formulation technology.

Generally, the dissolution property of a formulation containing a certain compound as an active ingredient varies depending on a variety of factors such as the chemical properties of the active ingredient, the composition of the formulations containing the active ingredient; the test conditions in a dissolution test such as the test medium, paddle speed and the like.

Nonetheless, Ishihara fails to teach or suggest the particular composition of the capsule of the present invention, the chemical properties of KMD-3213, and what test conditions such as the test medium and paddle speed should be used for conducting a dissolution test. Accordingly, one of ordinary skill in the art would not expect from the teaching of KMD-3213 and the number of ingredients listed in the specification in Ishihara that an 85% dissolution time of the capsule of the present invention could be not more than 15 minutes in a dissolution test according to method

2 (paddle method) of the Japanese pharmacopoeia under conditions using water as a test medium and a paddle speed of 50rpm.

Applicants respectfully submit that one of ordinary skill in the art would not have been led to the present invention from the combination of Kitazawa and Ishihara, given the extremely broad nature of the teaching in Ishihara.

Further, the capsule of the present invention has advantageous effects that could not be predicted from Ishihara. In order to demonstrate that the capsule of the present invention has unexpectedly superior and unpredictable advantages over Ishihara, Declarant Tsuyoshi Naganuma conducted tests for comparing dissolution rate as shown in the attached Declaration.

Ishihara discloses a tablet containing a) an active ingredient, b) lactose, c) corn starch and d) magnesium stearate as Formulation example 1. Declarant prepared a capsule using mannitol instead of lactose according to the tablet of Formulation example 1 as an Ishihara Comparative Example, and compared the dissolution rate of the capsule suggested by Ishihara with that of the capsule of the present invention. The results of dissolution tests clearly show that the capsule of Example 1 of the present application has much higher dissolution rate as compared with that of the capsule of the Ishihara Comparative Example which does not contain partially pregelatinized starch and sodium lauryl sulfate. Moreover, the capsule of Example 1 of the present application has much higher dissolution rate as compared with the capsule of Formulation H which does not contain sodium lauryl sulfate. Furthermore, significant filling problems during the encapsulating process were observed in the capsules of the Ishihara Comparative Example, whereas, the capsules of the present invention encountered no filling problems, and a good productivity was achieved.

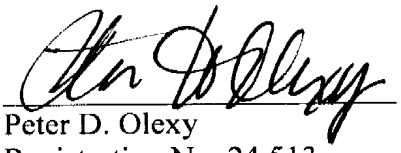
One of ordinary skill in the art could not predict such advantageous effects achieved by the capsule of the present invention from the teaching of Kitazawa and Ishihara.

Withdrawal and allowance are requested.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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